REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

1. Status of the Claims

Claims 16-23 were pending in this application when examined.

By this Amendment, claim 22 is cancelled.

2. Claim Rejections Under 35 USC § 103 Over Segers in view of Nakamura

The Examiner rejects claims 16-23 under 35 U.S.C. 103 (a) as being unpatentable over Segers et al. (US 5,383,324) ("Segers") in view of Nakamura et al. (US 6,867,193) ("Nakamura"). Claim 22 is cancelled, rendering its rejection moot. As applied to the remaining claims, Applicants respectfully traverse the rejection.

(2-1) Claim 16

(2-1-a) The Features of Claim 16

Claim 16 recites the following features:

(i) a first solution containing a potassium salt in a first chamber and a second solution containing a potassium salt in a second chamber;

(ii) the first solution and the second solution each have the same potassium salt; and

(iii) the first solution and the second solution each have a potassium ion concentration of about 2 to 40 mEq/L.

(2-1-b) The Unobviousness of the Features of Claim 16

Segers discloses on column 7, lines 42-50 that "when the solution contained in the upper chamber 44 is mixed with the solution contained in the lower chamber 46, the **subsequent** peritoneal dialysis solution has the following composition...0.0 to about 3.0 (mmol/L) potassium" (emphasis added).

Thus, the potassium ion concentration of "0.0 to about 3.0 mmol/L" disclosed in Segers is a concentration **after mixing a solution in an upper layer with a solution in a lower layer.**

Segers does not disclose or suggest a potassium ion concentration in the upper chamber, and does not disclose or suggest a potassium ion concentration in the lower chamber, **separately**.

Therefore, Segers does not teach or suggest feature (iii) of claim 16.

Further, Nakamura does not disclose or suggest that the first solution and the second solution each have the same potassium salt (feature (ii)), and the same potassium ion concentration of about 2 to 40 mEq/L (feature (iii)), as recited in claim 16. That is, Nakamura does not teach or suggest features (ii) and (iii) of claim 16.

Therefore, those skilled in the art would not have arrived at feature (iii), or the specific combination of feature (iii) with features (i) and (ii) of claim 16, from Segers in view of Nakamura.

Applicants submit herewith a Comparative Chart further explaining the differences between claim 16, Segers and Nakamura. As shown in the Chart, Segers does not mention feature (iii), and Nakamura does not mention features (i), (ii) or (iii).

Accordingly, the references do not teach or suggest features (i), (ii) and (iii) of claim 16.

(2-1-c) The Problem to be Solved by the Invention of Claim 16

In an infusion preparation in which a medicinal ingredient containing a potassium ion as an electrolyte at a high concentration is accommodated in one chamber of a plurality of chambers, a medical mistake in the communication operation will result in the administration of only one medicinal ingredient (a potassium ion having a high concentration) to the patient. When the potassium ion concentration is excessively high, the patient can develop hyperkalemia and, in the worst case scenario, the patient can die from cardiac arrest (see page 3, lines 20-29 of the specification).

Claim 16 is directed to an aseptic combination preparation which solves this problem, as disclosed on page 4, lines 15-18 of the specification.

Segers and Nakamura do not teach or suggest the above-mentioned problem, and thus the problem that claim 16 solves would not have been obvious over the references.

(2-1-d) The Unexpected Effects of the Invention of Claim 16

In the aseptic combination preparation of claim 16, the potassium ion concentration of each medical solution to be accommodated in a plurality of chambers is adjusted in a proper range, and there is no risk of causing hyperkalemia, etc. **As a result, the preparation of claim 16 will prevent the adverse effects on a living body from administering to a patient a medicinal solution of only one chamber of an aseptic combination preparation by mistake (see page 6, lines 6-15 of the specification).**

Thus, claim 16 achieves the remarkably superior effect of **preventing** adverse effects, such as hyperkalemia and cardiac arrest caused by medical mistakes.

Segers and Nakamura do not teach or suggest the remarkably superior effect of the invention of claim 16.

Rather, the purpose of Segers is to stabilize bicarbonate solutions (see column 3, lines 33-34 of Segers), and the purpose of Nakamura is to prevent an onset of hepatic encephalopathy caused by a conventional amino acid preparation, and to enhance the amelioration of the symptoms (see column 2, lines 1-4 of Nakamura).

The purposes and effects disclosed in Segers and Nakamura are quite different from the effect of eliminating adverse effects caused by a medical mistake. Therefore, the remarkably superior effect of claim 16 would not have been expected from Segers and Nakamura.

Accordingly, claim 16 would not have been obvious over the references.

Claims 17 and 18 depend from claim 16, and thus also would not have been obvious over the references.

(2-2) Claim 19

(2-2-a) The Features of Claim 19

Claim 19 recites the following features:

(i) a first solution containing at least one medicinal ingredient selected from the group consisting of a sodium salt, a sugar and a potassium salt in a first chamber and a second solution containing at least one medicinal ingredient selected from the group consisting of a sodium salt, a sugar and a potassium salt in a second chamber;

(ii) the first solution and the second solution each has the same medicinal ingredient; and

(iii) the first solution and the second solution each has an osmotic pressure ratio in the

range of about 1 to 3 relative to physiological saline.

(2-2-b) The Unobviousness of the Features of Claim 19

Nakamura discloses in Preparation Example 2 that "The above-mentioned amino acid solution A was...filled in a lower chamber of a double bag...On the other hand, the albumin preparation B...was filled in a lower chamber of the double bag...**When used, the two solutions in the double bag were mixed.** The drug solution **after they were mixed** had...an osmotic pressure ratio of 2.8 to 3.3" (see column 5, lines 44-53 of Nanamura, emphasis added).

Accordingly, the osmotic pressure ratio of 2.8 to 3.3 disclosed in Nakamura is a ratio after mixing the solution in the lower chamber and the solution in the upper chamber.

Thus, Nakamura does not disclose or suggest an osmotic pressure ratio of solutions in each of a lower chamber and an upper chamber (**i.e., in separate chambers**). Therefore, Nakamura does not teach or suggest feature (iii) of claim 19.

Segers does not teach or suggest an osmotic pressure ratio of a solution, and is thus silent regarding feature (iii) of claim 19.

Therefore, those skilled in the art would not have arrived at feature (iii), or the specific combination of feature (iii) with features (i) and (ii) of claim 19, from Segers in view of Nakamura.

As shown in the enclosed Comparative Chart, Segers does not mention feature (iii), and Nakamura does not mention features (i), (ii) or (iii) of claim 19. **Accordingly, the references do not teach or suggest features (i), (ii) and (iii) of claim 19.**

(2-2-c) The Problem to be Solved by the Invention of Claim 19

When the osmotic pressure ratio of a medicinal ingredient-containing solution is divided and accommodated in one chamber of a plurality of chambers and it is excessively high or low, and when the chambers are not communicated so that the medical ingredients are properly mixed, only the medicinal ingredient solution is administered to a patient. This causes severe vessel pain and destruction of erythrocytes in the blood (see page 3, last line - page 4, lines 8-18 of the specification).

Claim 19 provides an aseptic combination preparation which solves this problem, as disclosed on page 4, lines 15-18 of the specification.

Segers and Nakamura do not teach, suggest or even mention solving this problem.

Thus, the problem to be solved by the invention of claim 19 would not have been obvious in view of the disclosures of Segers and Nakamura. Thus, claim 19 would not have been obvious over the references.

(2-2-d) The Unexpected Effects of the Invention of Claim 19

In the aseptic combination preparation of claim 19, the osmotic pressure ratio of each medical solution in each chamber is adjusted in a proper range, and there is no risk of causing hemolysis due to low osmotic pressure, etc. As a result, the preparation of claim 19 prevents adverse effects on a living body by medical error, even if the medicinal solution in only one chamber is administered to a patient by mistake, as disclosed on page 6, lines 6-15 of the specification.

Therefore, the invention of claim 19 achieves superior and unexpected results over the references.

Segers and Nakamura do not teach or suggest the remarkably superior effects of claim 19.

Further, the effects of Segers and Nakamura, as mentioned in item (2-1-d) above, are quite different from preventing hemolysis and cardiac arrest.

Therefore, claim 19 would not have been obvious over the references.

3. Claim Rejections Under 35 USC § 103 Over Veech in view of Nakamura

The Examiner rejects claims 16-23 under 35 U.S.C. 103(a) as being unpatentable over Veech (US 5,200,200) in view of Nakamura. As applied to the remaining claims, Applicants respectfully traverse the rejection.

(3-1) Claim 16

(3-1-a) The Unobviousness of the Features of Claim 16

The Examiner states that "Exemplary solutions are taught by Veech in column 6, lines 11-39. Each of these solutions contains potassium ions up to 5 mM/L which is equivalent to 5 meq/L of potassium ions" (see Office Action, page 8, lines 18-20).

However, Veech discloses on column 6, lines 11-39 that "One class of exemplary solutions for use in such a technique comprises **parenteral solutions** having the following

composition:...Another class of exemplary solutions for use in such a technique comprises **peritoneal dialysis solutions** having the following composition:..." (emphasis added).

Those skilled in the art would not have found it obvious for one chamber of a container to accommodate a parenteral solution, and at the same, time the **other chamber** of the container to accommodate a peritoneal dialysis solution. **That is, the potassium ion concentration of 5 mM/L disclosed in Veech is not a concentration in each chamber, but a concentration after the contents of the chambers are combined and the solutions are mixed.**

Thus, Veech does not disclose or suggest that the first solution and the second solution each having the same potassium salt (feature (ii)), and that the first solution and the second solution each having a potassium ion concentration of about 2 to 40 mEq/L (feature (iii)), as recited in claim 16.

Further, Nakamura does not teach or suggest that the first solution and the second solution each have **the same potassium salt**, and each having **a potassium ion concentration of about 2 to 40 mEq/L**, as recited in claim 16. Thus, Nakamura does not teach or suggest features (ii) and (iii) of claim 16.

Therefore, one of ordinary skill in the art would not have arrived at features (ii) and (iii) of claim 16, and the specific combination of features (ii) and (iii), with feature (i) of claim 16, from Veech in view of Nakamura.

Moreover, as shown in the Comparative Chart, Veech and Nakamura do not mention features (i), (ii) or (iii).

Accordingly, the references do not teach or suggest features (i), (ii) and (iii) of claim 16.

(3-1-b) The Problem to be Solved by the Invention of Claim 16

Veech and Nakamura do not teach or suggest the problem which is solved by the invention of claim 16, as discussed in item (2-1-c) above (i.e., preventing medical errors).

Thus, the problem to be solved by the invention of claim 16 would not have been obvious from by the disclosures of Veech and Nakamura.

(3-1-c) The Unexpected Effect of the Invention of Claim 16

The invention of claim 16 achieves the remarkably superior effect of eliminating adverse effects, such as hyperkalemia on a living body, caused by medical mistakes as a result of the specific combination of features (i)-(iii) of claim 16, as mentioned in item (2-1-d) above.

Veech and Nakamura do not teach or suggest this remarkably superior effect.

Veech discloses effects of (a) maintaining two precursor components of a single solution **separately** during storage such that, **when the two components are to be used in a combined solution** dose form, there is a quick and easy technique for **selectively mixing such components** together in a closed container system under sterile conditions, thereby to provide a desired dose unit which is adapted for immediate administration (see column 2, lines 56-64 of Veech); (b) a method for [p]reparing a dose unit from two separate components, one of which contains metabolizable ketoacids and/or metabolizable sulfhydryl containing amino acids (see column 2, line 65-68 of Veech); (c) a method for preparing a dose unit of a therapeutic solution which contains a diffusable redox active component such as dissolved carbon dioxide and which, after storage, can be administered in a sterile condition without appreciable loss of the carbon dioxide (see column 3, lines 2-6 of Veech); and (d) redox active metabolite agents which are not deteriorated in component structure or concentration by storage before administration (see column 3, lines 8-11 of Veech).

These effects are quite different from the effect of eliminating adverse effects, such as hyperkalemia, on a living body caused by medical mistakes. Thus, the disclosure of Veech is quite different from the invention of claim 16.

Further, the effect of Nakamura is quite different from claim 16, as mentioned in item (2-1-d) above.

Thus, the disclosure, purposes and effects of Veech and Nakamura are quite different from the effect of the invention of claim 16. Therefore, the remarkably superior effect of claim 16 is quite unexpected to those skilled in the art.

Accordingly, claim 16 would not have been obvious over Veech in view of Nakamura.

(3-2) Claim 19

(3-2-a) The Unobviousness of the Features of Claim 19

As mentioned in item (2-2-b) above, Nakamura does not teach or suggest feature (iii) of claim 19, i.e., that the first solution and the second solution each have an osmotic pressure ratio in the range of about 1 to 3 relative to physiological saline.

Veech also does not teach or suggest an osmotic pressure ratio. Thus, Veech does not cure the deficiencies of Nakamura (see the Comparative Chart).

Therefore, those skilled in the art would not have arrived at feature (iii), as well as the specific combination of feature (iii) with features (i) and (ii) of claim 19, from Veech in view of Nakamura.

(3-2-b) The Problem to be Solved by the Invention of Claim 19

Veech and Nakamura do not teach or suggest the problem solved by the invention of claim 19, as mentioned in item (2-2-c) above (i.e., preventing medical errors).

Thus, the problem solved by claim 19 would not have been obvious or expected from the references.

(3-2-c) The Unexpected Effect of the Invention of Claim 19

The invention of claim 19 achieves a remarkably superior effect of eliminating adverse effects, such as hemolysis on a living body caused by medical mistakes, as a result of the specific combination of features (i)-(iii), as mentioned in item (2-2-d) above.

Veech and Nakamura do not teach or suggest the remarkably superior effect of the invention of claim 19.

Further, the effects of Segers and Nakamura, as mentioned in items (2-1-d) and (3-1-c) above, are quite different from the effect of claim 19. Thus, the effects of Veech and Nakamura are quite different from the effects of claim 19.

Accordingly, claim 19 would not have been obvious over Veech in view of Nakamura.

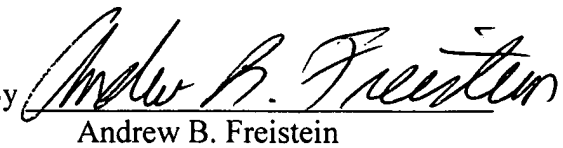
4. Conclusion

For these reasons, Applicants take the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing amendments and remarks, it is submitted that the rejections set forth by the Examiner have been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Nobuaki SUMIYOSHI et al.

By 

Andrew B. Freistein
Registration No. 52,917
Attorney for Applicants

WMC/ABF/vah
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
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Enclosure: Comparative Chart

Comparison between the present invention and the cited references

The invention of claim 16 Priority date: Jun. 6, 2003	D1: Veech (US 5,200,200) Date of patent: Apr. 6, 1993	D2: Nakamura et al. (US 6,867,193 B1) US filing date: Sep. 19, 2001	D3: Segers et al. (US 5,383,324) Date of patent: Jan. 24, 1995
An aseptic combination preparation to be mixed at the time of use by opening a partition wall which separates two or more chambers of a container, comprising	Methods are provided for preparing **just before administration unit doses of therapeutic solutions** (Abstract, lines 1-2); These separate component compositions are packaged in, for example, **individual chambers of a common sealed container which is so constructed as to permit the opening** --- **of a passage way between such chambers at the time when usage is contemplated** (Abstract, lines 9-14)	**When used, the two solutions** in the double bag **were mixed** (column 5, lines 51-52); a flexible plastic bag --- which comprises upper and lower chambers separated with a heat-sealed portion in a band-shape which **can easily peeled by strongly pressing the bag by hand** (column 4, lines 28-31); A vessel for containing the albumin preparation of the present invention includes --- **a plastic bag comprising** one or **two chambers** (column 4, lines 19-21)	In an embodiment, **the multi-chamber container 42 has a frangible seal 48 between the upper chamber 44 and the lower chamber 46**. **Opening the frangible seal 48 provides fluid communication between the upper chamber 44 and the lower chamber 46**. The multi-chamber 42 houses at least two non-compatible solutions that after mixture will result in **a ready-to-use** dialysis solution (column 7, lines 19-26)
a first solution containing a potassium salt in a first chamber and	**NO MENTION**	**NO MENTION**	In a preferred embodiment, **the upper chamber 44** can further include sodium chloride, **potassium chloride**, dextrose and dextrose polymers (column 7, lines 37-39)
	One class of exemplary solutions --- comprises **parenteral solutions** having the following composition: **Component** --- **K+** (column 6, lines 11-25)	**a required amount of** vitamins, --- electrolytes such as sodium, **potassium**, calcium, chloride, phosphorus, and trace elements --- **can be added to the albumin preparation** in the present invention (column 4, lines 1-7)	
a second solution containing a potassium salt in a second chamber,	**NO MENTION**	**NO MENTION**	Likewise, **the lower chamber 46** can further include **potassium chloride** (column 7, lines 39-41)
	Another class of exemplary solutions --- comprises **peritoneal dialysis solutions** having the following composition: **Component** --- **K+** (column 6, lines 26-40)	**a required amount of** vitamins, --- electrolytes such as sodium, **potassium**, calcium, chloride, phosphorus, and trace elements --- **can be added to the albumin preparation** in the present invention (column 4, lines 1-7)	
wherein the first solution and the second solution each have the same potassium salt	**NO MENTION**	**NO MENTION**	In a preferred embodiment, **the upper chamber 44** can further include --- **potassium chloride** ---. Likewise, **the lower chamber 46** can further include **potassium chloride** (column 7, lines 37-41)
and each have a potassium ion concentration of about 2 to 40 mEq/L.	**NO MENTION**	**NO MENTION**	**NO MENTION**
	One class of exemplary solutions --- comprises **parenteral solutions** having the following composition: **Component** --- **K+** --- **Quantity (in mM/liter)** --- **0-5** (column 6, lines 11-25); Another class of exemplary solutions --- comprises **peritoneal dialysis solutions** having the following composition: **Component** --- **K+** --- **Quantity (in mM/liter)** --- **0-5** (column 6, lines 26-40)		in an embodiment, **when the solution contained in the upper chamber 44 is mixed with the solution contained in the lower chamber 46, the subsequent peritoneal dialysis solution** has the following composition: --- **0.0 to about 3.0 (mmol/L) potassium** (column 7, lines 42-50)

The invention of claim 19 **Priority date: Jun. 6, 2003**	**D1: Veech (US 5,200,200)** **Date of patent: Apr. 6, 1993**	**D2: Nakamura et al. (US 6,867,193 B1)** **US filing date: Sep. 19, 2001**	**D3: Segers et al. (US 5,383,324)** **Date of patent: Jan. 24, 1995**
An aseptic combination preparation to be mixed at the time of use by opening a partition wall which separates two or more chambers of a container, comprising	Methods are provided for preparing **just before administration unit doses of therapeutic solutions** (Abstract, lines 1-2); These separate component compositions are packaged in, for example, **individual chambers of a common sealed container which is so constructed as to permit the opening** --- **of a passage way between such chambers at the time when usage is contemplated** (Abstract, lines 9-14)	**When used, the two solutions** in the double bag **were mixed** (column 5, lines 51-52); a flexible plastic bag --- which comprises upper and lower chambers separated with a heat-sealed portion in a band-shape which **can easily peeled by strongly pressing the bag by hand** (column 4, lines 28-31); A vessel for containing the albumin preparation of the present invention includes --- **a plastic bag comprising one or two chambers** (column 4, lines 19-21)	In an embodiment, **the multi-chamber container 42 has a frangible seal 48 between the upper chamber 44 and the lower chamber 46**. **Opening the frangible seal 48 provides fluid communication between the upper chamber 44 and the lower chamber 46**. The multi-chamber 42 houses at least two non-compatible solutions that after mixture will result in **a ready-to-use** dialysis solution (column 7, lines 19-26)
a first solution containing at least one medicinal ingredient selected from the group consisting of a sodium salt, a sugar and a potassium salt in a first chamber and	**NO MENTION**	**NO MENTION**	**the upper chamber 44** contains calcium chloride and magnesium chloride ---. In a preferred embodiment, **the upper chamber 44** can further include sodium chloride, **potassium chloride**, **dextrose** and **dextrose polymers** (column 7, lines 34-39)
	One class of exemplary solutions --- comprises **parenteral solutions** having the following composition: **Na+** **K+** --- HCO_3 (column 6, lines 11-19)	**a required amount of** vitamins, --- electrolytes such as **sodium**, **potassium**, calcium, chloride, phosphorus, and trace elements Also, nutrients such as **sugars** --- can be added (column 4, lines 4-10)	
a second solution containing at least one medicinal ingredient selected from the group consisting of a sodium salt, a sugar and a potassium salt in a second chamber,	**NO MENTION**	**NO MENTION**	**the lower container 46** contains bicarbonate. --- Likewise, **the lower chamber 46** can further include **sodium chloride**, **potassium chloride**, amino acids, peptides and glycerol (column 7, lines 36-41)
	Another class of exemplary solutions --- comprises **peritoneal dialysis solutions** having the following composition: **Component** **Na+** **K+** --- **glucose** (column 6, lines 26-40)	**a required amount of** vitamins, --- electrolytes such as **sodium**, **potassium**, calcium, chloride, phosphorus, and trace elements Also, nutrients such as **sugars** --- can be added (column 4, lines 4-10)	
wherein the first solution and the second solution each has the same medicinal ingredient and	**NO MENTION**	**NO MENTION**	In a preferred embodiment, the upper chamber 44 can further include **sodium chloride**, **potassium chloride**, dextrose and dextrose polymers. Likewise, the lower chamber 46 can further include **sodium chloride**, **potassium chloride**, amino acids, peptides and glycerol (column 7, lines 39-41)
each has an osmotic pressure ratio in the range of about 1 to 3 relative to physiological saline.	**NO MENTION**	**NO MENTION**	**NO MENTION**
		The --- **amino acid solution A** --- was filled in **a lower chamber of a double-bag** ---. On the other hand, **the albumin preparation B** --- was filled in **a lower chamber of the double bag** ---. When used, the two solutions in the double bag were mixed. **The drug solution after they were mixed** had --- **an osmotic pressure ratio of 2.8 to 3.3** (column 5, lines 44-53)	